



# Mitral valve replacement in patients under 65 years of age: mechanical or biological valves?

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## Purpose of review

There is controversy regarding the optimal choice of prosthetic valves in patients less than 65 years of age requiring mitral valve replacement (MVR). Recently, trends for valve replacement are moving towards biological prosthesis also in younger patients, which is justified by the fact that a later valve-in-valve procedure is feasible in the case of degeneration of the tissue valve. This strategy is increasingly recommended in aortic valve surgery but is questionable for MVR. The purpose of this review is to evaluate current guidelines and analyse evidence for biological MVR in patients under 65 years.

## Recent findings

There are differences between guidelines of the American Heart Association and those of the European Society of Cardiology concerning the choice of prostheses in patients undergoing MVR. Although the European Society of Cardiology recommends a mechanical mitral valve in patients under 65 years of age, the American Heart Association does not provide detailed advice for these patients. Mitral valve replacement with biological valves in patients under 65 years is associated with higher rates of reoperation due to structural valve deterioration. In addition, several studies showed a decreased survival after biological MVR.

## Summary

Evidence for biological MVR in patients less than 65 years without comorbidities or contraindication for oral anticoagulation does not exist. Recommendations for patients less than 65 years of age should not be blurred by current 'en-vogue' methods for promising but not yet proven valve-in-valve strategies.

## Keywords

mitral valve, structural valve degeneration, valve prosthesis

## INTRODUCTION

The use of biological or mechanical prosthetic heart valves for mitral valve disease is still a subject of debate in patients between the age of 60 and 70 years. According to the common evidence, mechanical valves are mainly selected for younger patients to avoid structural valve deterioration (SVD) [1<sup>st</sup>,2]. When surgical treatment of mitral valve disease is necessary, replacement of the valve is only performed when repair is not feasible or may expose the patient to an unacceptable risk of reoperation. According to the guidelines of the European Society of Cardiology, repair of the mitral valve is the method of choice in the large majority of patients [3<sup>rd</sup>,4]. When preservation of the native valve is, however, not possible, mitral valve replacement (MVR) can be achieved by either a mechanical or a biological valve prosthesis. The current guidelines uniformly recommend mechanical MVR in

patients under 60 years of age. In patients between 60 and 70 years of age, recommendations are, however, conflicting. Similarly to what is happening in aortic valve surgery, there is currently a trend to move towards more biological MVR – also in patients under 65 years of age. Justification for this approach is that the future option for later valve-in-valve procedure (in the case of SVD) is realistic. In addition, the last generation of pericardial tissue valves is expected to have a better long-term durability [4–7].

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## KEY POINTS

- Patients less than 65 years without comorbidities or contraindication to oral anticoagulation should receive a mechanical valve when the mitral valve has to be replaced.
- Valve-in-valve strategy is not proven to justify biological MVR at a younger age. Recommendations should not be blurred by current 'en-vogue' methods.

In the literature, biological MVR in patients under 65 years of age, however, results in higher rates of reoperation and decreased survival [1<sup>¶</sup>,2]. Valve selection is always a balanced decision, taking into account the pros and cons of both types of prostheses: limited durability of tissue valves and life-long requirement for anticoagulation with subsequent increased risk of bleeding and thromboembolic complications after mechanical valve replacement. Furthermore, the selection of the valve prosthesis depends on various patient-related factors, such as age of implantation, durability of the valve, compliance with long-term anticoagulation, and the patient's preferences.

## CURRENT GUIDELINES

In the 2014 guidelines (Table 1), the American Heart Association (AHA) recommends mechanical MVR in patients less than 60 years of age who do not have a contraindication to long-term anticoagulation [1<sup>¶</sup>,2]. In patients between 60 and 70 years of age, both biological and mechanical MVR are acceptable options according to these guidelines. Both recommendations are justified with a level of evidence (LOE) B and class of recommendation (COR) IIa. For patients older than 70 years, a biological valve prosthesis is recommended (LOE: B/COR: IIa). The only class I recommendation concerning type of prosthesis is the choice of a tissue valve for MVR independently of age in the case that anticoagulation is contraindicated (LOE: C/COR: I) [3<sup>¶¶</sup>,4].

In the 2012 guidelines of the European Society of Cardiology (ESC) (Table 1), mechanical MVR is indicated for all patients with a risk for accelerated SVD and in patients who already have a mechanical prosthesis in another position (LOE: C/COR: I) [1<sup>¶</sup>,4–7]. Unlike the 2014 AHA guidelines, the 2012 ESC guidelines precisely state that mechanical MVR should be considered in patients under 65 years of age (LOE: C/COR: IIa). The AHA guidelines are less precise and only mention a range of 10 years between 60 and 70 years of patient age where any decision is appropriate [1<sup>¶</sup>,2]. In patients with an

increased risk of SVD (e.g., end-stage renal disease [ESRD] or hyperparathyroidism), mechanical MVR is recommended (LOE: C/COR: I). Only the 2012 ESC guidelines suggest a mechanical prosthesis as an optimal choice in patients with a reasonable life expectancy for whom future reoperation due to SVD would be associated with a high risk (LOE: C/COR: IIa). In both the guidelines, the patient's choice is considered a class I recommendation [1<sup>¶</sup>,4].

## CURRENT EVIDENCE

The choice between a mechanical and a biological valve in adults is generally determined by the assessment of the risks of anticoagulation-related bleeding and thromboembolism in patients with a mechanical valve against the risk of SVD in those patients with a tissue valve. In addition, the patient's opinion and his estimated quality of life as health-care preferences are considered. Structural valve degeneration is clearly dependent on the age at implantation and the position of the tissue valve (mitral earlier than aortic).

Hammermeister *et al.* [8] reported a long-term follow-up of 181 patients who underwent biological MVR with the Carpentier–Edwards PERIMOUNT mitral prosthesis (Edwards, Irvine, CA, USA): a very low rate of reoperation because of SVD was observed in patients who received the tissue valve at an age lower than 65 years (freedom from reoperation of 76.8% at 15 years). In contrast, when MVR was performed in patients younger than 65 years, they had a freedom of only 49.5 and 25.1% from reoperation because of SVD at 15 and 20 years, respectively.

In one of the most cited studies, the Edinburgh heart valve trial, the mitral valve was replaced in 261 patients, the aortic in 211, and both valves in 61 patients [9]. After 20 years of follow-up, no difference between the survival rates of the two groups was observed. The reoperation rate was higher for the biological group, whereas more patients with a mechanical heart valve experienced a bleeding complication due to anticoagulation.

In the randomized Veterans Affairs trial, 575 men received either a mechanical Bjork–Shiley or a biological Hancock prosthesis (394 aortic valve replacement and 181 MVR) [8]. After a follow-up of 15 years, survival rate was higher in the group of patients who received mechanical MVR. Bleeding complications were more frequent in patients with mechanical valves, but no significant difference was observed for thromboembolic and infectious complications. As expected, SVD occurred more frequently in younger patients who received a tissue valve: in 26% of patients who received aortic valve

**Table 1.** Comparison between guidelines for the treatment of patients with valvular heart disease of the American Heart Association/American College of Cardiology and the European Society of Cardiology

Guidelines	AHA/ACC			ESC		
	COR	LOE	Age	COR	LOE	Age
Choice of valve intervention should be a shared decision process with the patients	I	C	No limitation	I	C	No limitation
Type of valve prosthesis is recommended according to the desire of the informed patient	I	C	No limitation	I	N	No limitation
Mechanical prosthetic mitral valve	Ila	B	<60	Ila	C	<65
Biological prosthetic mitral valve	Ila	B	>70	Ila	C	>70
Mechanical prosthesis in patients at risk for accelerated SVD	n/c	n/c		I	C	<40
Mechanical prosthesis in patients already under anticoagulation for a mechanical valve prosthesis	n/c	n/c		I	C	No limitation
Bioprosthesis is recommended for patients at any age for whom anticoagulation is contraindicated	I	C	No limitation	I	C	No limitation
Either a mechanical or a bioprosthetic valve is reasonable	Ila	B	60–70	n/c	n/c	
Bioprosthesis in patients with desire to have children	n/c	n/c		Ila	C	No limitation

ACC, American College of Cardiology; AHA, American Heart Association; COR, class of recommendation; LOE, level of evidence; n/c, not clarified; SVD, structural valve deterioration.

replacement with a tissue valve under 65 years of age but 44% after MVR with a tissue valve in patients under 65 years of age.

A retrospective study by Hanania [10] in a homogeneous patient cohort, separated by the year of intervention, length of follow-up, and age at the time of surgery between 60 and 70 years, showed similar results to those reported by the Veterans Affairs trial. Among the 574 patients enrolled, a subgroup received 184 prosthetic mitral valves (99 mechanical and 85 biological). Overall survival was better in patients receiving mechanical prosthetic valves.

These reports can be interpreted as a confirmation of the European guidelines that consider the cutoff limit of 65 years to recommend a mechanical prosthesis (<65) or a biological prosthesis (>65).

## BLEEDING

Patients who undergo valve replacement with a mechanical prosthesis receive life-long oral anticoagulation therapy to prevent thromboembolic events. This treatment is associated with an increased risk of bleeding [11]. The absolute risk of anticoagulation-related intracranial haemorrhage is between 0.3 and 1% per year, compared with a spontaneous rate of 0.15% per year [12]. In addition, these patients have an annual risk of thromboembolic events of 1–2% compared with 0.7% in those patients who receive a tissue valve [3<sup>\*\*\*</sup>].

Kaneko *et al.* estimated the freedom from major bleeding in patients under 65 years of age after mechanical MVR as 87.2, 79.2, and 71.2% at 5, 10, and 15 years, respectively [2]. In the group with biological MVR, freedom from major bleeding

at 5, 10, and 15 years was 91.1, 85.0, and 77.9%, respectively.

Surprisingly, these differences were not statistically significant [2] and the results were confirmed in other studies [13]. In patients older than 65 years, the use of biological MVR has been supported by the low rate of SVD and haemorrhagic complications [14,15].

## RENAL INSUFFICIENCY

Chronic renal disease is associated with a higher incidence of cardiovascular calcifications and represents an independent risk factor for all-cause mortality [16]. Incidence of malnutrition, inflammatory state, atherosclerosis, and calcium–phosphorus metabolic disorders with substantial calcifications of native heart valves is significantly higher in patients with ESRD [17].

The reduced life expectancy of these patients – when compared with the normal population – makes the choice of the optimal valve prosthesis a subject to debate.

The traditional view of the American College of Cardiology/AHA was that tissue valves may undergo accelerated calcification leading to premature SVD in patients with ESRD. Therefore, mechanical valves have been recommended as the better choice in these patients. In 2004, the Canadian Cardiovascular Society Consensus on Surgical Management of Valvular Heart Disease recommended bioprostheses for valvular replacement surgery in patients with ESRD because of their significantly reduced life expectancy [18]. Nevertheless, there is still controversy regarding optimal recommendation for valve selection in patients with ESRD requiring dialysis. Zhibing *et al.* [19<sup>¶</sup>] reported no significant difference of early and late mortality in patients on chronic renal replacement therapy independently of the valve implanted. In addition, no premature SVD was reported after biological valve replacement [19<sup>¶</sup>].

The 2012 ESC guidelines acknowledge in this specific situation that tissue valve should be considered in patients whose life expectancy is lower than the presumed durability of the prosthesis. Furthermore, biological valve replacement is recommended in patients in whom comorbidities may necessitate further surgical procedures, and in patients with increased risk of bleeding [4]. Patients with chronic renal failure have an impaired long-term survival after heart valve replacement regardless of the implanted prosthesis (biological or mechanical). This observation and an increased risk of complications (bleeding, thromboembolism, and infection) with mechanical valves may favour the choice of a tissue valve in this situation [19<sup>¶</sup>].

The 2006 AHA guidelines already recognized that mechanical valve replacement may be a source of problems in patients with renal failure and those on dialysis. Chronic dialysis patients tend to have more haemorrhagic complications. Therefore, these patients, when they receive long-term anticoagulation therapy, may be at an increased risk for bleeding, and current recommendations clearly favour a bioprosthesis in patients with ESRD [18,20–22]. The limited life expectancy in patients with ESRD, even under the age of 65 years, justifies the implantation of a bioprosthetic valve [23,24].

## VALVE CHOICE IN WOMEN OF CHILD-BEARING AGE

The selection of the ideal prosthesis is a major difficulty in patients with the desire to have children. All types of prosthetic valve can cause significant problems during pregnancy. The 2012 ECS guidelines emphasized the high risk of thromboembolic complications with a mechanical prosthesis during pregnancy despite correct anticoagulation [4,25]. A planned pregnancy is considered a class IIb and a level C evidence indication for a biological valve [4,23].

The rapid development of SVD in this age group, however, is a limiting factor to the durability of the tissue valves, and controversy exists as to whether pregnancy *per se* may lead to accelerated SVD [18,20,22]. These patients will all need a reoperation if they received a tissue valve, but the risk of peri-operative mortality is between 0 and 5%. In comparison, the spontaneous risk of mortality in pregnant patients with a mechanical valve is estimated to be around 1–4% [23].

The risks of anticoagulation should be thoroughly discussed with the patient when pregnancy occurs. In the first trimester, the respective maternal and fetal risks (e.g., teratogenicity) should be carefully assessed. During the second and third trimesters, phenprocoumon is favoured until the 36th week. A recent review of the literature confirmed the low risk of valve thrombosis with oral anticoagulation throughout pregnancy (2.4%, 7/287 pregnancies) compared with unfractionated heparin (UFH) in the first trimester (10.3%, 16/156 pregnancies) [25]. From the 36th week, phenprocoumon should be replaced by heparin until delivery [23].

## CONCLUSION

The survival rates of patients following mechanical and biological valve replacement are comparable. The current trend in the literature is moving towards



the implantation of bioprosthetic valves in younger patients (<65 years of age). This trend is justified by the improved durability of the current generation of tissue valves and the technical feasibility of a subsequent valve-in-valve procedure (in the case of degeneration of the tissue valve) to avoid open-heart surgery. Although this might appear reasonable in high-risk and elderly patients, this approach is not supported by scientific evidence in younger patients, especially not for those without comorbidities or contraindication for anticoagulation. There are, however, certain patient groups under 65 years of age in whom tissue valve is a good option for MVR: those with contraindication to anticoagulation, those with ESRD, and, of course, women with the wish for pregnancy.

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## Conflicts of interest

There are no conflicts of interest.

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- of special interest
- of outstanding interest

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